

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 16 December 1999 (16.12.99)	
International application No. PCT/CA99/00449	Applicant's or agent's file reference 74268-28
International filing date (day/month/year) 19 May 1999 (19.05.99)	Priority date (day/month/year) 19 May 1998 (19.05.98)
Applicant SAWYNOK, Jana et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

01 December 1999 (01.12.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election
- ☒
- was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:

MORROW, Joy D.  
SMART & BIGGAR  
P.O. Box 2999, Station D  
900-55 Metcalfe Street  
Ottawa, Ontario K1P 5Y6  
CANADA

Date of mailing  
(day/month/year) 05.07.2000

Applicant's or agent's file reference  
74268-28

**IMPORTANT NOTIFICATION**

International application No.  
PCT/CA99/00449

International filing date (day/month/year)  
19/05/1999

Priority date (day/month/year)  
19/05/1998

Applicant  
DALHOUSIE UNIVERSITY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

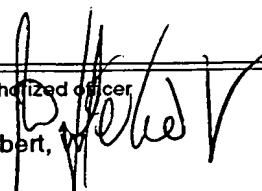
#### 4. REMINDER


The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/  
European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer  
Hebert,   
Tel. +49 89 2399-2152



*Handwritten initials: JBM*

# PATENT COOPERATION TREATY

## PCT

REC'D 07 JUL 2000

WIPO

PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>74268-28</b>	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. <b>PCT/CA99/00449</b>	International filing date (day/month/year) <b>19/05/1999</b>	Priority date (day/month/year) <b>19/05/1998</b>	
International Patent Classification (IPC) or national classification and IPC <b>A61K31/645</b>			
Applicant <b>DALHOUSIE UNIVERSITY</b>			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand <b>01/12/1999</b>	Date of completion of this report <b>05.07.2000</b>
Name and mailing address of the international preliminary examining authority:  <b>European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465</b>	Authorized officer <b>Economou, D</b> Telephone No. +49 89 2399 8599



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

because:

- ☒ the said international application, or the said claims Nos. 1-25, 54-62, 68 (see separate sheet, item 1) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☒ the description, claims or drawings (indicate particular elements below) or said claims Nos. 13-17, 21-23, 42-43, 49-53, 55-57, 62-64, 66-71 (see separate sheet, item 3) are so unclear that no meaningful opinion could be formed (specify):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Inventive step (IS)

Industrial applicability (IA)

2. Citations and explanations

see separate sheet

Yes: Claims 4, 6, 18, 31, 50, 52, 56  
No: Claims 1-3, 5, 7, 12, 19-20, 24-30, 32-41, 44-48, 51, 54, 63, 65 (see separate sheet, item 3)

Yes: Claims 4, 6, 18, 31, 50, 52, 56  
No: Claims 1-3, 5, 7, 12, 19-20, 24-30, 32-41, 44-48, 51, 54, 63, 65 (see separate sheet, item 3)

Yes: Claims 1-25, 54-62, 68 (see separate sheet, item 2a); 26-53, 63-67, 69-71 (see separate sheet, item 2b)  
No: Claims

No: Claims

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

## I. Basis of the report

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

Description, pages:

as originally filed

1-50

Claims, No.:

as originally filed

1-53

54-71

Drawings, sheets:

as originally filed

1/23-29/29

2. The amendments have resulted in the cancellation of:

- ☐ the description,  
☐ the claims,  
☐ the drawings,

pages:  
Nos.:  
sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

4. Additional observations, if necessary:

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious) or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application  
☒ claims Nos. 1-25, 42-43, 49, 53-62, 64, 66, 68-69, 71

06/06/2000

06/06/2000 with letter of

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA99/00449

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-50 as originally filed

**Claims, No.:**

1-53 as originally filed

54-71 as received on 08/06/2000 with letter of 06/06/2000

**Drawings, sheets:**

1/29-29/29 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 1-25,42-43,49,53-62,64,66,68-69,71.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA99/00449

because:

- ☒ the said international application, or the said claims Nos. 1-25,54-62,68 (see separate sheet, item 1) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 13-17,21-23,42-43,49,53,55,57-62,64,66-71 (see separate sheet, item 3) are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	4,6,18,31,50,52,56
	No:	Claims	1-3, 5,7-12,19-20,24-30,32-41,44-48,51,54,63,65 (see separate sheet, item 3)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	4,6,18,31,50,52,56 (see separate sheet, item 3)
Industrial applicability (IA)	Yes:	Claims	1-25, 54-62, 68 (see separate sheet, item 2a); 26-53,63-67,69-71 (see separate sheet, item 2b)
	No:	Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA99/00449

- 1). Claims 1-25,54-62 and 68 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
- 2).
  - a). For the assessment of the present claims 1-25,54-62 and 68 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
  - b). The subject-matter of claims 26-53,63-67 and 69-71 fulfils the requirements of industrial applicability.
- 3). Claims 42-43 are unclear due to their dependence to claim 23 which is a use claim and does not relate to a composition.

The term "polymer stabilized crystal" used in claims 21,23,49,53,55,57,60,62,64,66,69 and 71 is unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

The term "second generation or third generation antidepressant" is not clear since it does not unambiguously define which antidepressants fall within this category. Hence, the subject-matter of claims 58-62, 67-71 is not clear (Art. 6 PCT). The same objection applies also to the subject-matter of claim 1 (and dependent claims thereto) for which however an opinion was given on the basis of the term "tricyclic" antidepressants and on the basis of the compounds explicitly disclosed or defined by a formula.

The formula defined in claim 13 is unclear (see formula mentioned in the description from page 18, line 16 to page 19, line 10). The same applies also to

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/CA99/00449

claims 14-17 and 22 due to their dependence to claim 13.

- 4). According to the description (see page 6, last paragraph and page 7, second paragraph) the topical formulations of the present application include inter alia saline solutions or injections.

**D1** (=ORTEGA-ALVARO A. ET AL.: "The effects of different monoaminergic antidepressants on the analgesia induced by spinal cord adrenal medullary transplants in the formalin test in rats" ANESTHESIA AND ANALGESIA, vol. 84, no. 4, April 1997 (1997-04), pages 816-820, USA) discloses on page 817, left column, second paragraph, injections comprising amitriptylin or desipramine in a sterile saline solution. As far as an injection solution is suitable for local administration, the subject-matter of claims 26-29,32-36,45,47-48 and 51 is not novel.

Following the same argumentation (see above) the subject-matter of claims 26-30,32-36,45,47-48 and 51 is not novel since **D2** (=SIERRALTA, F. ET AL.: "Effect of p-Chlorophenylalanine and alpha-Methyltyrosine on the Antinociceptive Effect of Antidepressant Drugs" PHARMACOLOGY AND TOXICOLOGY, vol. 77, no. 4, October 1995 (1995-10), pages 276-280, DK) discloses on page 277, left column, forth paragraph and right column, lines 3-7, injectable solutions comprising clomipramine hydrochloride, imipramine hydrochloride or maprotiline methanesulfonate.

The subject-matter of claims 37-41 is not novel since **D4** (=WO-A-91/02527; not cited in the ISR; a copy was attached to the first written opinion) discloses compositions for topical administration comprising trazodone (see page 4, last four lines; claims 1,3-5,10,13 and 14).

The subject-matter of claims 37-39 is not novel since **D5** (=EP-A-0 431 663; not mentioned in the ISR; a copy of the document was attached to the first written opinion) discloses a buffered aqueous solution of mirtazapine comprising NaCl (see column 4, first paragraph).

**D3** (=WO-A-97/10815) relates to the use of topically applied compositions used for the treatment of pain, especially sympathetically mediated pain (see page 1,



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/CA99/00449

last paragraph to page 4, last paragraph), regardless of cause (see abstract). The method utilizes the periodic application of topical compositions containing three classes of therapeutically effective agents prepared in suitable bases, to the skin areas affected by the pain. The three classes of therapeutic active agents are NMDA receptor antagonists, anticholinergic agents (inter alia amitriptyline; see page 11, last paragraph) and sympathetic blocking agents. Each can be used alone or in combinations (see abstract). The compositions may comprise lecithin as an penetration enhancer (see page 13, third paragraph and page 15, first paragraph). Response and mechanism of action of the compositions are disclosed from page 16, last paragraph to page 17, first paragraph; page 17, last paragraph to page 18, first paragraph; page 18, last paragraph; see experimental results from page 20 to page 24 with compositions comprising amitriptyline (composition no.3) or compositions comprising a combination of amitriptyline with ketamine (composition no.5), from page 25 to page 30, first paragraph and claims 1,3,5,7,9,11,13,15,17,20,22.

In the light of **D3** the subject-matter of claims 1-3,5,7-11,19,20,24-28,32-36,44-46,48,54,63 is not novel since all its technical features are already known from **D3**.

The subject-matter of claims 4,6,18,29-31,47,50,52,56 and 65 which is formally novel over **D3** does not involve an inventive step since the use of tricyclic antidepressants for producing local analgesia by local administration at the site of local discomfort is obvious from the said document (see analysis of the document above).

With the same technical problem (treatment of SMP by topical administration; see abstract; see page 1, line 8 to page 2, line 3; see page 4, penultimate paragraph; ) deals also **D6** (=WO-A-92/14453; not cited in the ISR; a copy of the document was attached to the first written opinion). **D6** discloses topical compositions comprising nefazodone or trazodone for the treatment of SMP (see claims 1,15,16 and claims 38-40) administered as lotions, ointments, solutions, transdermal patches or administered by iontophoresis (see claims 38-40). In the light **D6** the subject-matter of claims 1,12,37-41 is not novel since all its technical features are disclosed in the said document (see analysis of the document above).

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11.08.08.00

ART 34 AMDT

60

54. A method for producing local analgesia in a subject having a site of local discomfort, said method comprising locally administering an effective amount of a tricyclic antidepressant to the site.

5

55. The method according to claim 54 wherein the antidepressant is administered as a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a polymer stabilized crystal, a powder, and an aerosol.

10

56. The method according to claim 54 wherein the antidepressant is administered by a method selected from supersonic powder injection, and transdermal electroporation.

15

57. The method according to claim 54 wherein the antidepressant is administered encapsulated in a delivery system selected from the group consisting of a microsphere, a polymer stabilized crystal, and a liposome.

20

58. A method for producing local analgesia in a subject having a site of local discomfort, said method comprising locally administering an effective amount of a second generation or third generation antidepressant to the site.

25

59. The method according to claim 58, wherein the antidepressant is administered by injection.

30

60. The method according to claim 58 wherein the antidepressant is administered as a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a polymer stabilized crystal, a powder, and an aerosol.

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ART 34 AMDT

N 08.08.08  
61

61. The method according to claim 58 wherein the antidepressant is administered by a method selected from supersonic powder injection, and transdermal electroporation.

5 62. The method according to claim 58 wherein the antidepressant is administered encapsulated in a delivery system selected from the group consisting of a microsphere, a polymer stabilized crystal, and a liposome.

10 63. The use, in the manufacture of a medicament, of a tricyclic antidepressant, as an active ingredient in a composition for producing local analgesia when administered at a site of local discomfort, in admixture with an inert carrier.

15 64. The use according to claim 63 wherein the antidepressant is administered as a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a polymer stabilized crystal, a powder, and an aerosol.

20 65. The use according to claim 63 wherein the antidepressant is administered by a method selected from supersonic powder injection, and transdermal electroporation.

25 66. The use according to claim 63 wherein the antidepressant is administered encapsulated in a delivery system selected from the group consisting of a microsphere, a polymer stabilized crystal, and a liposome.

30 67. The use, in the manufacture of a medicament, of a second generation or third generation antidepressant, as an active ingredient in a composition for producing local analgesia when administered at a site of local discomfort, in admixture with an inert carrier.

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ART 34 AMDT

N 08.08.00  
62

68. The method according to claim 67, wherein the antidepressant is administered by injection.

69. The use according to claim 67 wherein the antidepressant is administered as a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a polymer stabilized crystal, a powder, and an aerosol.

70. The use according to claim 67 wherein the antidepressant is administered by a method selected from supersonic powder injection, and transdermal electroporation.

71. The use according to claim 67 wherein the antidepressant is administered encapsulated in a delivery system selected from the group consisting of a microsphere, a polymer stabilized crystal, and a liposome.

add  
C<sup>3</sup> 7

add  
dl<sup>3</sup> 7

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

SMART & BIGGAR  
Attn. MORROW, Joy D.  
P.O. Box 2999, Station D  
900-55 Metcalfe Street  
Ottawa, Ontario K1P 5Y6  
CANADA

ON  
DOCKET

*Journal to 13/1/99  
RT d to Oct 1/99  
Comp. note d*

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

01/09/1999

Applicant's or agent's file reference

74268-28

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/CA 99/ 00449

International filing date  
(day/month/year)

19/05/1999

Applicant

**DALHOUSIE UNIVERSITY**

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Heike Zoglauer

*gfm*

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>74268-28</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/CA 99/ 00449</b>	International filing date (day/month/year) <b>19/05/1999</b>	(Earliest) Priority Date (day/month/year) <b>19/05/1998</b>
Applicant <b>DALHOUSIE UNIVERSITY</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

**4. With regard to the title,**

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

**USE OF TRICYCLIC ANTIDEPRESSANTS FOR LOCAL ANALGESIA**

**5. With regard to the abstract,**

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. The figure of the drawings to be published with the abstract is Figure No.**

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.



## INTERNATIONAL SEARCH REPORT

National Application No

T/CA 99/00449

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K31/645 A61K31/55

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 01157 A (THE WWK TRUST) 15 January 1998 (1998-01-15) page 1, line 4 - line 11 page 2, line 1 - page 3, line 7 page 4, line 11 - line 22 page 8, line 7 - line 19 page 11, line 23 - line 27 claims 1-5,8,9,12,13,16,19,20 --- -/--	1-53



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

13 August 1999

Date of mailing of the international search report

01/09/1999

Name and mailing address of the ISA

 European Patent Office, P.B. 5818 Patentlaan 2  
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Authorized officer

Economou, D

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CA 99/00449

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 10815 A (FROME, B.) 27 March 1997 (1997-03-27) claims 1,3,5,7,9,11,13,15,17,20,22 page 20, line 1 - page 31, paragraph 3 page 18, paragraph 3 - page 19, paragraph 1 page 17, last paragraph - page 18, line 3 page 16, last paragraph - page 17, paragraph 1 page 15, paragraphs 1,3 page 13, paragraph 3 page 11, last paragraph page 9 page 5, paragraph 4 page 1, line 1 - page 4, line 6	1-53
X	ORTEGA-ALVARO A. ET AL.: "The effects of different monoaminergic antidepressants on the analgesia induced by spinal cord adrenal medullary transplants in the formalin test in rats" ANESTHESIA AND ANALGESIA, vol. 84, no. 4, April 1997 (1997-04), pages 816-820, XP002112201 usa page 817, left-hand column - page 820, left-hand column, line 23 page 816, right-hand column abstract	1-53
X	SIERRALTA, F. ET AL.: "Effect of p-Chlorophenylalanine and alpha-Methyltyrosine on the Antinociceptive Effect of Antidepressant Drugs" PHARMACOLOGY AND TOXICOLOGY, vol. 77, no. 4, October 1995 (1995-10), pages 276-280, XP002112202 denmark page 277, right-hand column, line 10 - page 279, right-hand column, paragraph 5 page 277, left-hand column, paragraphs 4,6 page 276, left-hand column, paragraph 3 - page 276, right-hand column, paragraph 3 abstract	1-53